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METHODACCORDINGTO.USPT,PGPB.	1
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Term	Documents
L-SELECTIN.USPT,PGPB.	416
L-SELECTINS.USPT,PGPB.	33
CD34.USPT,PGPB.	719
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<u>DB Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
USPT,PGPB	'l-selectin' same cd34	34	<u>L4</u>
USPT,PGPB	method\$ same cd34 .clm.	43	<u>L3</u>
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USPT,PGPB	lasky-laurence\$	25	<u>L1</u>

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L4: Entry 25 of 34

File: USPT

Jul 20, 1999

US-PAT-NO: 5925349

DOCUMENT-IDENTIFIER: US 5925349 A

TITLE: Treating inflammation via the administration of specific sulfatase enzymes and/or sulfation inhibitor

DATE-ISSUED: July 20, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Rosen; Steven D.	San Francisco	CA		
Hemmerich; Stefan	San Francisco	CA		
Imai; Yasuyuki	Tokyo			JPX

US-CL-CURRENT: 424/94.61; 424/662, 424/702, 424/94.1, 424/94.6, 435/196, 435/200

CLAIMS:

We claim:

1. A method of treating inflammation resulting from the binding of L-selectin to a sulfated L-selectin ligand, said method comprising:
administering to a patient a pharmaceutical preparation comprising a therapeutically effective amount of an inhibitor of sulfation and a sulfatase enzyme; and
allowing the inhibitor to inhibit the sulfation of a saccharide molecule within a naturally occurring selectin ligand.
2. The method of claim 1, wherein the inhibitor blocks formation of 3' phosphoadenosine 5' phosphosulfate.
3. The method according to claim 2, wherein said inhibitor is a selenate.
4. The method according to claim 3, wherein said selenate is sodium selenate.
5. The method according to claim 2, wherein said inhibitor is a chlorate.
6. The method according to claim 2, wherein said chlorate is sodium chlorate.
7. A method of treating inflammation resulting from the binding of L-selectin to a sulfated L-selectin ligand, said method comprising:
administering to a patient a pharmaceutical preparation comprising a therapeutically effective amount of a selenate and a sulfatase enzyme; and
allowing said selenate to inhibit the sulfation of a saccharide molecule within a naturally occurring selectin ligand.
8. The method according to claim 7, wherein said selenate is sodium selenate.
9. A method of treating inflammation resulting from the binding of L-selectin to a sulfated L-selectin ligand, said method comprising:
administering to a patient a pharmaceutical preparation comprising a therapeutically effective amount of a chlorate and a sulfatase enzyme; and
allowing said chlorate to inhibit the sulfation of a saccharide molecule within a naturally occurring selectin ligand.
10. The method according to claim 9, wherein said chlorate is sodium chlorate.

WEST**End of Result Set**

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L4: Entry 34 of 34

File: USPT

Jan 23, 1996

US-PAT-NO: 5486536

DOCUMENT-IDENTIFIER: US 5486536 A

TITLE: Sulfatides as anti-inflammatory compounds

DATE-ISSUED: January 23, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ward; Peter A.	Ann Arbor	MI		
Miyasaka; Masayuka	Suita			JPX
Suzuki; Yasuo	Shizuoka			JPX

US-CL-CURRENT: 514/460

CLAIMS:

What is claimed as new and is desired to be secured by Letters Patent of the United States is:

1. A method of treating selectin-dependent lung inflammation in a patient in need thereof comprising, administering an effective amount of a sulfatide.
2. The method of claim 1, wherein said sulfatide is a brain sulfatide.
3. The method of claim 2, wherein said sulfatide is bovine brain sulfatide.
4. The method of claim 1, wherein said sulfatide is of the formula (I):
##STR2## where R is SO.sub.3 ; and
R.sup.1 is --(CH.sub.2).sub.n --CH.sub.3 where n is an integer of from 10 to 30.
5. The method of claim 4, wherein n is of from 20 to 30.
6. The method of claim 5, wherein n is 30.
7. The method of claim 1, wherein said sulfatide is a sulfatide ganglioside.
8. The method of claim 1, wherein said effective amount is 1.0 to 3.0 mg/kg based on the body weight of the patient.
9. The method of claim 1, wherein said administration is performed 1 to 5 times per day.
10. The method of claim 1, wherein said sulfatide is administered to the airway of said patient.
11. The method of claim 10, wherein said sulfatide is administered in the form of a pharmaceutically acceptable aerosol spray.
12. The method of claim 1, wherein said sulfatide is administered intravenously.

WEST**End of Result Set**

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L4: Entry 34 of 34

File: USPT

Jan 23, 1996

DOCUMENT-IDENTIFIER: US 5486536 A

TITLE: Sulfatides as anti-inflammatory compounds

BSPR:

Besides the family of oligosaccharides that are reactive with lectin binding sites on selectins, additional ligands are also known. These include sulfated glycolipids (such as sulfatides and seminolipids) (Y. Suzuki, et al., Biochem. Biophys. Res. Comm. 190, 426 (1993)), a sulfated and sialylated mucin-like molecule which is present in high venular endothelial cells of lymph nodes and has been termed Gly-CAM-1 (L. A. Laskey et al., Science 361, 555 (1993); L. A. Laskey et al., Cell 69, 927 (1991)), a sulfated heparin-like molecule extracted from endothelial cells (K. E. Nogard-Sumnicht, et al., Science 261, 480 (1993)), sulfated glycans (fucoidin, dextran sulfate) (L. M. Stoolman, et al., Cell. Biol. 99, 1535 (1984); T. A. Yednock, et al., J. Cell. Biol. 104, 713 (1987)), a sulfoglucuronyl glucosphingolipid (Needham and Schnaar, Proc. Nat'l. Acad. Sci. USA, 90, 1355 (1993)), CD34 sialomucin (S. Baumhueter et al., Science 262, 436 (1993)), and sulfated oligosaccharides (such as sialyl Lewis^{sup.x} and sialyl Lewis^{sup.a}) (C-T. Yuen et al., Biochem. 31 9126 (1992)). Most of these lectins are reactive with L-selectin, while binding to P- and E-selectin has been variously reported (G. Todderud et al., J. Leukoc. Biol. 52, 85 (1992)). Virtually nothing is known regarding the in vivo blocking activity of these compounds in acute inflammatory reactions.

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L4: Entry 33 of 34

File: USPT

Feb 6, 1996

US-PAT-NO: 5489578

DOCUMENT-IDENTIFIER: US 5489578 A

TITLE: Sulfated ligands for l-selectin and methods of treating inflammation

DATE-ISSUED: February 6, 1996

US-CL-CURRENT: 514/61; 514/25, 514/53, 514/54, 514/62, 536/17.2, 536/18.7,
536/4.1, 536/53, 536/54, 536/55, 536/55.1, 536/55.2

APPL-NO: 8/ 432849

DATE FILED: May 2, 1996

PARENT-CASE:

RELATED APPLICATIONS This application is a continuation of U.S. application Ser. No. 08/155,947 filed Nov. 19, 1993, now abandoned, which we claim priority under 35 USC .sctn. 120 and which is incorporated herein by reference.

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L4: Entry 33 of 34

File: USPT

Feb 6, 1996

DOCUMENT-IDENTIFIER: US 5489578 A

TITLE: Sulfated ligands for l-selectin and methods of treating inflammation

BSPR:

Presently, the best characterized ligands are the HEV-associated ligands for L-selectin, known as GlyCAM-1 (previously termed Sgp50) and Sgp90 (Imai, Y., Singer, M. S., Fennie, C., Lasky, L. A., and Rosen, S. D., J. Cell Biol., 113:1213-1221 (1991)). These endothelial-associated ligands are mucin-like glycoproteins with sulfated, sialylated and fucosylated O-linked oligosaccharide chains and were originally detected by precipitation of lymph node extracts, metabolically labeled with ³⁵S, with a soluble L-selectin/immunoglobulin chimera. Other lower affinity ligands may exist that fail to be precipitated by the chimera but nonetheless participate in functionally significant interactions in the context of cell-cell binding events (Berg, E. L., Robinson, M. K., Warnock, R. A., and Butcher, E. C. J. Cell. Biol., 114:343-349 (1991)). GlyCAM-1 is released into conditioned medium of cultured lymph nodes as an intact molecule (Lasky, L. A., Singer, M. S., Dowbenko, D., Imai, Y., Henzel, W. J., Grimley, C., Fennie, C., Gillett, N., Watson, S. R., and Rosen, S. D., Cell, 69:927-938 (1992); Brustein, M., Kraal, G., Medius, R. E., and Watson, S. R., J. Exp. Med., 176:1415-1419 (1992)), suggesting that it is a secreted product and/or a loosely associated peripheral membrane component. In contrast, Sgp90 is an integral membrane protein, requiring detergent for extraction (S. Hemmerich and S. Rosen, unpublished results). Molecular analysis has revealed GlyCAM-1 to be a novel mucin-like glycoprotein, and more recently Sgp90 has also been shown to be an HIV-specific glycoform of the mucin CD34, Baumhueter, S., Singer, M. S., Henzel, W., Hemmerich, S., Renz, M., Rosen, S. D. and Lasky, L. A., Science, 262:436-438 (1993). GlyCAM-1 and Sgp90 are sulfated, fucosylated, and sialylated glycoproteins (Imai, Y., and Rosen, S. D., Glycoconjugate J., 10:34-39 (1993)). The O-linked chains of GlyCAM-1 have been shown to be heterogeneous in both size and charge. Some of the chains bear multiple charges, the major contribution apparently coming from sulfation rather than sialylation. The interaction of both GlyCAM-1 and Sgp90 with L-selectin depends on their sialylation, confirming earlier findings that sialidase treatment of lymph node HEV impairs lymphocyte attachment and lymphocyte trafficking (Rosen, S. D., Singer, M. S., Yednock, T. A., and Stoolman, L. M., Science, 228:1005-1007 (1985); Rosen, S. D., Chi, S. I., True, D. D., Singer, M. S., and Yednock, T. A., J. Immunol., 142:1895-1902 (1989)). However, exhaustive desialylation does not completely abrogate the ligand activity of GlyCAM-1, suggesting that a sialic acid-independent mode of recognition also exists (Imai, Y., Lasky, L. A., and Rosen, S. D. Glycobiology, 4:373-381). The sialic acid which forms part of the ligand binding site of GlyCAM-1 appears to be in an α 2-fwdarw.3 linkage, since the linkage-specific sialidase from Newcastle disease virus partially inactivates GlyCAM-1 as a ligand. Furthermore, both in competitive inhibition studies and direct binding studies, sLe^x-type oligosaccharides manifest ligand activity for L-selectin whereas the Lewis X-type structures with α 2-fwdarw.6 linked Neu5Ac are inactive (Foxall, C., Watson, S. R., Dowbenko, D., Fennie, C., Lasky, L. A., Kiso, M., Hasegawa, A., Asa, D., and Brandley, B. K., J. Cell Biol., 117:895-902 (1992)). An essential contribution from fucose is suspected, since sialyllactose (i.e., Neu5Ac. α 2-fwdarw.3Gal. β 1-fwdarw.4Glc) as compared to sLe^x is relatively inactive as a competitor of L-selectin binding. Moreover, fucose has been shown to be a critical determinant for the neutrophil ligands for P-

and E-selectin (Larsen, G. R., Sako, D., Ahern, T. J., Shaffer, M., Erban, J., Sajer, S. A., Gibson, R. M., Wagner, D. D., Furie, B. C., and Furie, B., J. Biol. Chem., 267:11104-11110 (1992)), and in light of the sequence similarity among the lectin domains of the selectins is likely to be important for L-selectin ligands as well.

DEPR:

Sgp50 has recently been molecularly cloned and shown to be a mucin-like glycoprotein with extensive O-linked carbohydrate chains. Sgp50 has been given the designation GlyCAM-1. Sgp90 is a HEV-specific glyco-form of CD34. Sialic acid on both Sgp50 and Sgp90 is required for their interaction with L-selectin. Several fortuitous carbohydrate-based inhibitors of L-selectin such as fucoidin and sulfatide are sulfated. Sulfate is required (but not sufficient) for binding activity (Imai et al., Nature, 361:555-557 (1993)). Examples exist where sulfate modifications of carbohydrate chains are essential for ligand activity (Lerouge et al., Nature, 344:781 (1990); Fiete et al., Cell, 67:1103).

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L4: Entry 33 of 34

File: USPT

Feb 6, 1996

US-PAT-NO: 5489578

DOCUMENT-IDENTIFIER: US 5489578 A

TITLE: Sulfated ligands for l-selectin and methods of treating inflammation

DATE-ISSUED: February 6, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Rosen; Steven D.	San Francisco	CA		
Hemmerich; Stefan	San Francisco	CA		

US-CL-CURRENT: 514/61; 514/25, 514/53, 514/54, 514/62, 536/17.2, 536/18.7,
536/4.1, 536/53, 536/54, 536/55, 536/55.1, 536/55.2

CLAIMS:

We claim:

1. A sulfated, sialylated, fucosylated O-linked oligosaccharide compound of formula I(a): ##STR5## wherein GlcNAc is N-acetylglucosamine, Gal is galactose, Sia is sialic acid, Fuc is fucose and X is a moiety connected to the 1-position of GlcNAc selected from the group of --OH, a detectable label and a pharmaceutically active drug.

2. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 1.

3. A method of treating inflammation comprising administering to a patient in need of such a therapeutically effective amount of the composition of claim 2.

4. The method as claimed in claim 3, wherein the composition is administered by injection.

5. The method of claim 3, wherein the composition is administered by inhalation.

6. A compound of structural formula I(c): ##STR6## wherein X.sub.(c) is a moiety connected to GalNAc at the 1-position selected from the group of --OH, a detectable label and a pharmaceutically active drug.

7. A pharmaceutical composition comprising a pharmaceutically acceptable excipient carrier and a therapeutically effective amount of a compound of claim 6.

8. A method of treating inflammation comprising administering to a patient in need of such a therapeutically effective amount of the composition of claim 7.

9. A compound of structural formula I(d): ##STR7## wherein X.sub.(d) is a moiety connected to GalNAc at the 1-position selected from the group of --OH, and detectable label and a pharmaceutically active drug.

10. A pharmaceutical composition comprising a pharmaceutically acceptable excipient carrier and a therapeutically effective amount of a compound of claim 9.

11. A method of treating inflammation comprising administering to a patient in need of such a therapeutically effective amount of the composition of claim 10.

12. A compound of structural formula I(e): ##STR8## wherein X.sub.(e) is a moiety connected to GalNAc at the 1-position selected from the group of --OH, a detectable label and a pharmaceutically active drug.

13. A pharmaceutical composition comprising a pharmaceutically acceptable excipient carrier and a therapeutically effective amount of a compound of claim 12.

14. A method of treating inflammation comprising administering to a patient in need of such a therapeutically effective amount of the composition of claim 13.

15. A sulfated, fucosylated O-linked oligosaccharide compound having the structural formula II; ##STR9## wherein GlcNAc is N-acetylglucosamine, Gal is galactose, Sia is sialic acid, Fuc is fucose and X is a moiety connected to the 1-position of GlcNAc selected from the group of --OH, a detectable label and a pharmaceutically active drug.

16. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 15.

17. A method of treating inflammation comprising administering to a patient in need of such a therapeutically effective amount of the composition of claim 16.

18. A compound having a structure selected from the group consisting of:
##STR10##